Introduction and guest background

Welcome, everybody, to this edition of the Exponential Longevity Summit. I'm your host, Doctor Jeffrey Gladden. And as always, we're here discussing how we leverage AI to outlive disease and live beyond for a lifetime.

And today, I'm joined by a very interesting physician. Doctor Austin Perlmutter. He's an internal medicine board certified physician. He's a New York Times bestselling author.

He's published, he's a published researcher and international educator. And he's, he's got an interest in longevity. So with that, Austin, welcome to the show.

Thanks so much for having me. Yeah. So, Austin, tell us a little bit about, your journey from internal medicine into longevity. That's not necessarily a straight path.

Yeah. You know, there are many ways to get into this. I think the fundamental reconceptualize ation that I had as to what interests me and what I think is important around health, is the movement away from surrogate outcomes to primary outcomes.

And what I mean by that is medicine can seem like an incredibly siloed field. And I mean, I guess it is, you know, you have a cardiologist working on your heart, a gastroenterologist working on your GI tract, a pulmonologist working on your lungs.

And between all of these doctors, there are so many things that we care about. So respiratory function, blood pressure or GI function. As an internal medicine doctor, I was really tasked with trying to integrate all this information to prevent, but largely to manage chronic diseases.

Brain health as the core of longevity

And the bottom line here is the understanding that in the modern world, the majority of death and disability comes from chronic and largely preventable diseases.

So we chase the things that we think are related to those conditions. We try to bring down blood pressure. We try to work on every part of the body. But when I was sitting across from patients in the clinic, I had the recognition that the biggest issues that were driving diseases were things happening outside the doctor's office.

And in particular, the only thing that mattered was state of mind. And why I say that is because whether it's blood pressure or GI dysfunction or any other surrogate we could look at in terms of health, it only matters because at the end of the day, it hopefully leads to improvements in our mental health because our ability to enjoy our lives, to experience quality over the years we have on this planet is kind of the only thing that matters.

That is a reflection of brain health. So when I put all of this together, I understood that majority of what I was learning and applying in the clinic was relevant in terms of understanding the biology that was driving disease and may allow us to work on prevention, but was insufficient in the context of understanding that if brain health was the most important thing, then I didn't really understand what was driving people to good brain health or bad brain health, which subsequently led to mental health conditions and subsequently led to decision making.

Could they start exercising or not? These are a function of our brain state. And so the the framework that I, I move towards and where I operate now is saying that the goal is to maximize quality of brain function for the most years possible.

So it's area under the curve. It's not a question of great brain health today, terrible brain health tomorrow. It is

maximal or maximum brain health over the most years possible.

You know, it's a no. It's just for a second. So I really like your comment about how, as physicians are trained to focus on surrogate markers, right? I mean, if the audience says you're listening to this, a surrogate marker is basically an approximation of what it is you're trying to actually take care of.

Like, for example, if you want to take care of your water heater, the surrogate marker would be either what's the temperature or what's the water pressure, but it's not actually telling you what's the status of of the water heater, right.

Whether there's rust or whether there's contamination or mold or any. It's not that it's basically a surrogate marker. And so likewise in medicine, we're trained to look at surrogate markers.

What's your cholesterol, what's your blood pressure, etc. as if that's an indicator of underlying health. And in in a way it is. But it's also important to understand that it is a surrogate.

It's not really looking at what's really going on with the water here. Right. And then the other thing that that I've come to realize, and you and I are meeting for the first time now, but the book I wrote, 100 is a new 30.

We talk about five circles. Four circles, actually life energy, right. Which is a whole psycho spiritual space. Longevity itself. All the drivers of aging, all the hallmarks of phenotypic expressions are drivers and all the health related issues, and then all the performance related issues.

Fast, agile, strong, quick balance. Right. And I've come to realize that quite honestly, all of life comes down to one thing. And I have this conversation with my with my clients all the time.

All of life comes down to one thing, and they look at me a little askance, like, really? If it comes down to one thing, and I said, yes, it comes down to one thing.

It's optimizing the nervous system, right? Think what you feel, what you believe to be true, what you think is possible, what you're living in, reaction to, how you move, how you run, how you do it all.

It's we. We isolate the brain from the rest of it's one nervous system, as you know. Well, no. Right. So, I mean, we really have one nervous system. And so there is no this peripheral versus central is really an artificial demarcation.

So I think that really life to echo really what you're saying it all comes down to optimizing your nervous system, which is, you know, cognitively brain function.

So anyway, just to let you know, we're on the same page. Absolutely. I mean, I think anybody who sits with it long enough will come to that same realization.

And the exercise I like to have people kind of go through is to say, what is it that you care about? And people will say different things. I want to make money.

I want to be happier in my relationship. I want to live a long time. I want to have less knee pain. If you ask why, why do you want that?

Three brain systems that drive healthspan

Eventually it all gets back to you. Because it makes me feel good, because it improves my brain state. And so the fundamental point here is to say, if we can better understand what is leading our brains to a state of balance or imbalance, then we can act on the primary driver of what is most important in terms of anything that matters for human health.

And so with that reframe in mind, what longevity represents to me isn't just this function of how many years can we

live, which I think is the popular conception of the topic.

I just want to live a long time. It's a question of what is the maximum area under the curve, meaning the quality combined with the variable of quantity of the years that we can have on this planet.

And so I had been primarily focused on the idea of brain health span, which is similar to brain longevity, but it brings in the additional variable of saying it's not just about the number of years.

And I've had the experience of having multiple family members who have had Alzheimer's disease. And so I recognize very acutely that there is a difference between being alive and in a nursing home and barely functional, and being alive and able to enjoy the time that we have on this planet.

And so for any of these things that matter, I mean, personally, I would rather live more healthy years than more unhealthy years. I think that's obvious, but I think that it may be better to live less healthy years than more unhealthy years.

In a perfect scenario, we're optimizing for both. So again, my focus has been in trying to get people to understand that the health span of their brain, the number of years, and the quality of those years of their brain is the most important variable that matters.

And the things that we can do to more successfully optimize our lives towards maximizing that outcome. Yeah, I think that's exactly right. The way I would summarize that is, the target for longevity for us is a 30 year old body at 100, a 30 year old body and a 300 year old mind.

Right? Okay. All the wisdom, all the insight, all the equanimity. Right? All the spiritual insight, all the connection, all the relationships. Right. Because I think we focus to your point.

We focus a lot on physical health and we negate or or certainly as isn't addressed and certainly as an address, some of most longevity practices, the whole what I would call psycho spiritual space, which includes the cognitive.

But to your point around mindset and you know, what makes you happy and things like that, right? So, so anyway, yeah, 30 year old body, 300 year old mind.

So again, I think we're on the same page. So very, very cool. So how do you go about doing that? I primarily focus on three systems within the brain that are not only fundamental to how we think, act and feel, but are modifiable by our lifestyle.

And there are many other systems within the brain, but I think these are three that allow us to understand where things go wrong. And to intervene to enhance our chances of things going right.

And those three systems are going to be brain metabolism or neuro metabolism, basically, how our brain uses energy, neuro immunity, and in particular inflammation within the brain.

So how our brains immune system functions and whether it goes towards a state of relative inflammation. And the third is neuroplasticity, which is the study of how our brain changes in response to our environment. Yep.

And within the Venn diagram of those three systems, I think we can have an amazing understanding of how brain diseases develop. Specifically, the most common neurodegenerative diseases of the day.

And here I'm primarily focused on dementia, which affects about 60 million people around the world, a number that is expected to increase to 150 million by 2050, as well as age related cognitive decline, which I don't even know if we should call it that.

But around one third of people after the age of 85 will have mild cognitive impairment, not quite dementia, but a decrease or a drop off in their brain function.

We've kind of assumed that as we age, our brain function should get worse. I don't necessarily agree with that. But again, this is in part a reflection of these three systems converging.

And then the other pieces would be, things like mental health. So depression in particular tends to be a condition that preferentially affects women and also may affect the elderly, at higher levels than the adult, However, it also seems to anxiety and depression affect younger people far more than it used to.

Depression, we now understand, is no longer a serotonin issue, and rather maybe a function of these three domains the, energetic with metabolism, the immune with neuro immunity, and then the neuro plastic conditions, it extends over into stress and how people handle or don't handle stress.

Stress, trauma, and nervous system safety

We know stress conditions are among the top sources of poor mental health around the world, affecting at least a billion people. So this is a major issue.

And then the final piece would be day to day brain function and decision making. This is a, an incredibly important variable that is largely ignored, which is that the quality of our lives is a reflection of the quality of our decision making and our decision making.

Meaning do we get up in the morning and go for a jog, or do we get up in the morning and eat? An unhealthy breakfast? Is a function of these systems within the brain our metabolic, our immune and neuroplasticity states.

So I find that starting there and helping people to appreciate how these three systems can be compromised by our lives is actually the best way to get people into, consideration around protecting their brains against what usually happens as we age.

And, again, optimizing brain health span over the years that we have left on this planet. Yeah, I agree with that. You know, in the life energy circle, where we kind of talk about this, I think one of the things that I would bring up is the fact that with stress.

Right, anxiety, stress, anger, fear, concern, worry, I think all those things. And correct me if if you think I'm wrong here, but in my thought process around us, I think most of those things, if not all of them, really double down to not feeling safe.

And so when people start to understand that there's nothing external to them that will ever make them feel safe, because history shows us that everything we have can be taken away right?

So there's nothing external, Lewis that can ever make us feel safe. So then how do you actually give yourself safety, right? How do you actually give yourself safety?

That becomes a psycho spiritual question. That's one thing. I mean, I'll just leave it at that. If you want to share. Well, let me comment on that. I really love that framework.

What I would say is, historically and for reasons that are no longer valid, we have separated out psychological and biological processes. So we'd say a person's experiencing stress.

That's a psychological issue. And then we'd say a person is experiencing Alzheimer's. It's a biological issue. So in Alzheimer's, there's a buildup of amyloid in stress, though, it's a person just, you know, not handling the outside world.

What I would say is a better, more copasetic way of looking at, how the environment impacts our brain for the worse, or just in general, is that our brains are tasked with detecting danger and data from the outside world, and we can conceptualize that through the lens of psychological threat, or we conceptualize that through the lens of internal threat.

So in many ways, it's a conversion pathway. Meaning if you were to turn on the news and watch something horrible happening in a distant part of the, the world, your brain still sees that as danger.

It still sees that as an existential threat, and it activates the same cascade of chemicals that may be activated through eating the unhealthy food, which your body and your brain then interprets as a danger signal.

So to your point, you know, our brains function differently depending on the data that they receive. And I think it's really key to appreciate that if we want longevity of good brain function, it's not a question of having no stress.

It's not a question of having no danger in the absence of any sort of external danger or stressful stimuli. Our brains and our bodies will adapt to a low energy state.

And that's actually quite unhelpful for us, because one of the things that we see consistently in the literature is the people who have optimal brain function for the longest amount of time are those who are perpetually experiencing some degree of brain stress.

Now, that doesn't necessarily mean that they're being stressed because they're watching the news each day. That actually means that they're stressing their brains by learning a new language, or putting themselves in situations that are novel or doing things that their brains don't necessarily know how to respond to.

Easily working can actually be a very positive stressor. There's a reason why retirement is actually correlated with a number of negative outcomes in terms of health.

Because when we are telling our brains there's something that we need to do, that brain becomes active and it uses, it synapses, it uses its network in a way that is different from the brain that is not being used in that way.

That said, coming back to kind of the central point, I do think it is the case that one of the most caustic, influences on long term brain health is the perpetual intake of a danger signal that can be from psychological stress, that can be from inflammatory molecules produced by our diet.

That can be because our brains are never being told that they have time to clean themselves out and rebalance themselves because we're not getting good sleep.

But the basic idea here being that our brain function is a reflection of what happens in our outside environment and our inside environment, and we can have agency over what that data looks like.

But if we keep our brain in a perpetual state of unhealthy danger, signaling that is exactly what leads to worse mental health, worse cognitive health worth decision making, and overall much lower quality of life.

Right? I couldn't agree more. And obviously, brain function, biological function, it's all integrated, right? The circles I have are all interrelated, like Venn diagrams with, life energy, the one that binds them all.

I think, you know, the other interesting thing is I think about this, is that people grow up and they've experienced certain traumas. Right. And certain ways. Right.

I don't know of anybody that didn't grow up and experience of trauma, loss of a parent, somebody getting sick, you know, blah, blah, whatever it was, being bullied, whatever it might be.

And we tend to live in reaction to those traumas. And so it sort of sets our amygdala up. It sets up our sensing system to actually recognize danger in places where as an adult, the danger may not exist.

And so actually, I think part of the solution, too, is going back and actually unraveling those traumas to actually understand why are we living on tilt?

Why are we biased towards being more anxious that the person next to us, when the same stimulus comes in the

bus drives by one person scared to death, the other person is no big deal, right? So.

So I think being able to go in and actually solve those issues, has a direct impact on biology as well. So so let me dive into that a little bit. And you feel free to pull me back out if we go too deep.

So one of the the incredible things about our brains is that they're always changing. One of the incredibly dangerous things about our brains is that they're always changing.

What I tell people is your brain is different today than it was yesterday, and tomorrow will be a different brain. This sense we have of a stable identity, that's the same me waking up each day is actually an illusion because our brains are perpetually rewiring themselves and even growing new brain cells.

So coming back to the point you made things that happen early in our life, there's a period of relatively high plasticity, specifically through our childhood, but the brain's really still kind of programing itself all the way into our mid-twenties in terms of major structural and functional change.

These things have an outsize effect on how we think, act, and feel in the years to come. This is one of the reasons why adverse childhood events, adverse childhood experiences, or aces, seem to have such an outsize effect on mental health cognitive health later in life.

But one of the questions that we have been asking, kind of across the field of understanding brain influences over the lifespan is how does that happen?

And so we might just say, oh, I have this really traumatic memory, or I had this, this thing happened a long time ago and I still experience it. But the question is where and why.

Epigenetics, plasticity, and brain reprogramming

So where in the brain is that experience and why do we keep having that experience every time we see something similar to it? Usually the way that it's been kind of described, and what I think still really learned in medical training is that to act on those pathways or sorry to act on those memories, there are two options.

One is you put somebody in to talk therapy and you help them work through the things that happened earlier in life. And the other one is you look at medications so the person has perpetual anxiety, a kind of a PTSD type of experience because they experience problems in the past, traumas in the past.

We can think about, pharmaceutical interventions. And granted, there are others, eMDR and other things kind of in between. But again, talk to a person in a way to kind of help them see things in a different way or potentially medicate in a way of acting on those biological pathways.

But it doesn't get to the core question of why is it stored in the brain for so long? Where does that storage exist? And one of the, breakthroughs in recent research that has completely changed the way that we look at basically every condition, but especially brain health conditions, is the understanding that trauma, as well as just general life experiences, both external and internal effects of those experiences, the way that this is stored within our brains is through a process called epigenetics.

So epigenetics, can be a little bit complicated, but the basic idea behind epigenetics is that it's not just about our DNA. We used to think you had DNA, and then you had life experiences, and those two things maybe bumped into each other a little bit, but they didn't exactly communicate.

And now what researchers are telling us is that the way our DNA is used is modified by the lives that we live. So these are changes that occur on our DNA.

They don't mess with the actual DNA sequence, but they modify not even a binary on off, but more like a dimmer switch. The extent to which that DNA gets transcribed or programed into, basically pathways that change our

brains.

So yeah. Putting this together for a moment, our life experiences change the way that our DNA is used. And this may be one of the reasons why events like trauma have such a lasting effect on our brain function.

Now then the question would be, well, what do we do about this? So the first step is to understand how the DNA is being changed. And a number. So now looked at.

And this is incredibly germane to longevity in general. The marking on our DNA is a better predictor of lifespan than the number of years we've lived.

Meaning if you understand epigenetics, it tells you more about, your risk for developing something like an age related condition and how long you're going to live, then just knowing your age and birthdays.

This is the trade off between, typical ways of understanding aging and a biological way of understanding aging. So that's really important. But within the brain, what is fascinating to me is that as we look at some of these conditions, for example, PTSD, we think if it is partially epigenetic in terms of why it's programed into the brain, are there interventions that can act on this?

And this has been proposed, actually, as one of the mechanisms behind the science, showing that MDMA, which is, a form of psychedelic therapy for people with PTSD, why that might be efficacious.

And we're actually looking in a small study now on the effects of another psychedelic ayahuasca on epigenetics, because we know that people who use psychedelics can have enduring benefits to mental health, but we don't necessarily know why.

And epigenetics has emerged as one of the potential kind of through lines in that. Now, to take that one step, I guess back beyond psychedelics, because it's not necessarily what I'm recommending here in terms of brain longevity.

Everything that we do that acts on our physiology, may have an effect on epigenetics. So the food that we eat, the exercise that we get, whether we calorie restrict or not, the quality of sleep we get, the stress we experience.

All of these things can be interrogated using epigenetics. And what we're looking at here is, could certain interventions lead to long term benefits in part through their epigenetic expression.

So that's a lot of science a little bit of complexity here. But the. Good. The main point I would make for people is to understand that this, this domain that we've usually seen has relatively, inflexible, rigid, which is you get a certain set of DNA from your parents, and there's really nothing that you can do about that.

You know, you hope it doesn't mutate. But other than that, you just say your DNA is what it is over the lifespan that it may be, equally important and in many cases, more important, not what the DNA is, but rather how that DNA is being used.

And that is the domain in which we have agency. We can make changes to influence those markings that then change the way the DNA is being used. Yeah, I agree completely.

I think, you know, the epigenetics really sort of is the record keeper on one hand of what's happened. And we know this to be true with trauma, you know, even that is passed down through generations.

Right. There's famous studies about the Dutch that were invaded, by Germany. And then, you know, the children that were in utero at that time, how they had significantly increased health consequences, more anxiety, more depression, not just those, but actually other health consequences and died sooner.

And their children also were impacted by that. So the epigenetics, as I see it, are it's kind of a record keeper of

what's going on. It's but it's only one record keeper because it also expresses itself in the neural pathways.

Right? In terms of what's wired to fire, so to speak. It's also, for example, the muscles. It's, you know, epigenetics if you exercise, yes, it's in the genes, but your muscle also gets bigger and stronger, more flavor.

So there's there's a physiologic, imprint of it. There's the epigenetic imprint of it. There's, you know, the metabolic imprint of it. So all these things kind of come together in an orchestrated way.

And you're nodding your head because we're on the same page here. But I think to your point, what's fascinating is that it is the reprograming of the nervous system, that I think this is why, for me, it comes down to one thing, which is how do you optimize the nervous system?

That is, the metabolic is a big piece of that, of course, is is neuroplasticity and decreasing inflammation. I found that almost all neurodegenerative diseases are a function of neuroinflammation.

That seems to be a common thread. Right. So there are other nuances to it of course. But this idea of reprograming the nervous system and and and doing it with, you know, combinations of therapies, there is value to cognitive support.

We can know that many people that can only take us so far, you know, things like transcranial magnetic stimulation, a lot of forms can do certain things.

Right. You know, eMDR can do things and, and but looking at this as how do we actually optimize this system, across all of it and ultimately, to your point, then we end up modifying the epigenetics.

And that has a massive impact on longevity and health going forward, not just for us, but if we're young enough. And that's a big impact on our offspring too, which is a very that's right. That's right.

Sure. There's a lot to to talk about here. One thing I will just say is that if we look at epigenetics, it's incredibly complicated. This is where AI and machine learning are, are at their best because, we just did a study, and for each person, we looked at 850,000 locations of epigenetic change.

So at the start and at the end, so over 1.5 million sites per person, and we had 50 people. And there's no human that's going to spend the time necessary to compare all of those.

So without powerful, algorithms, there's no way to to really put all this together. But to your point, in terms of, you know, what do we do about it? I think this is a balance, right?

So a lot of what I'm talking about here is designed to get people to say, oh my gosh, I didn't know about this science and I didn't know about the opportunity post.

I didn't realize that I can change my brain, that it is always evolving over the lifespan, that I can grow new brain cells, and if I do that, it's going to enhance my brain function.

I'm going to think clearer, I'm going to feel better. I'm going to protect my brain against Alzheimer's disease. So the first part, I think, is the inspiration and the excitement around knowing that you are the most important person when it comes to your brain health, that nobody else in the world, doctors included, has a as powerful an opportunity to improve brain function and keep it healthy over the lifespan than you, and therefore it is fully, you know, kind of your opportunity to make some of these changes to prevent conditions like Alzheimer's, to enhance mood, to protect good cognition.

And the second part of this is to say, well, what do I do about this? Right. Because, okay, I'm I'm inspired, I'm excited. What do I do about this? And I think the the challenge can be there are so many things that we could talk about.

Everything from hyperbaric oxygen therapy to supplementation to, ketogenic diet. All of these things are part of the conversation. So I guess I'll defer to you here.

We could talk about, you know, a general kind of protocol in terms of the most important things for most people, we could go deep into neuro immune, neuro metabolic, neuro plastic.

But I want to make sure we leave people with a couple of things that they can do right now that are most, kind of evidence based to support brain healthspan.

Yeah. You know, in, in, in the work that we do, what we find to be really helpful, in every situation, and everybody needs work in this regard that we, that we come into contact with.

I haven't met anybody yet that that doesn't need some help in this regard is to actually deconstruct a situation before we start making recommendations.

So doing testing, you know, what are your epigenetics, right. What's your epigenetics around your brain for that matter? These are testable.

Exercise, creatine, and brain energy

You know, what's your cognitive ability currently. Right. What's your what's your emotional state. What's your how much anxiety depression things like that.

If you can actually deconstruct a situation, actually see what it is you're dealing with initially, then all of a sudden it's like, oh, okay, well here's the opportunities.

These these will have these things. Maybe hyperbaric is the best thing because you just had a concussion, but maybe there's some problem. Maybe it's something over here where, you know, some maybe a psychedelic would be good, or maybe talk therapy or maybe a combination of exercise and whatever else.

Right. So you're getting your diet, right. Because that's the number one thing that's killing you. So, for me, I'm a big fan of kind of deconstructing it before we kind of make the recommendations.

So that's that's just how we think. But I like that. I also appreciate the thousands of people who are going to be watching this, and not everyone has access to a practitioner who's going to be able to walk them through those things.

And so what I will usually say is both the brain, I would say definitely important for people to work with practitioners, especially if you're somebody who is really struggling with brain health, you're a person who would benefit most from working with a person, for a practitioner.

So, for example, somebody saying, I'm incredibly depressed and I can't get out of bed, that's not the person I want to say, well, I'll just start exercising and call it a day.

That's the person who really needs to call up and get assistance from a professional. But I also think, you know, maybe if I could just float a couple of really interesting new studies, new research that correlates to some of these systems. So one of the things that I become very, very excited about is the role of specific forms of exercise in protecting and enhancing brain function.

And so we've known for a long time that people who exercise tend to do better across basically every health metric. And we have, promoted for decades the idea of jogging, aerobic conditioning in terms of cardio vascular risk prevention.

But what the research has told us, really, just in the last decade, is that when we activate large skeletal muscles, we produce molecules called myo kinds.

These are small chemical signals produced again by large skeletal muscles. And that myo kinds, which have names like I reason gets abs and B can actually reach the brain and influence brain, metabolic, brain, immune and neuro plastic pathways.

Now, what makes that interesting is in part the science behind it, but it's also the research suggesting that we can target myosin production with specific forms of exercise, and that this is linked to better brain health.

So obviously, my general recommendation here is that everyone shoot for getting their exercise 30 minutes or so a day or five days a week. But resistance training and activation in particular of the largest skeletal muscles in your body, which are in your lower extremities.

So your legs is probably the best way to enhance these machines. And a study came out in 2022 looking at one very interesting myocardium called brain drive neurotrophic factor, finding that of all the exercises that had high intensity interval training, they did aerobic conditioning, they did stretching, they did balance training.

Resistance training was linked to the highest levels of brain drive, neurotrophic factor in people's bloodstream, Bdnf. This brain derived neurotrophic factor levels go down and depression levels go down in Alzheimer's.

And it's believed that if we can increase those levels, it may positively, influence brain function. So the bottom line to all of this research would be as we're looking at exercise protocols to sustain brain health, lifting heavy things with your legs and specifically activating those large muscle groups is a wonderful way to enhance a person's exercise routine.

So that's just one one little bit of interesting kind of science. And a tidbit in terms of saying, ideally, you're getting 20 to 30 minutes of resistance training each week and really prioritizing your lower extremities, leg muscles, which for some people may be something they have not done before and therefore maybe they should work with a trainer.

The other thing that I think is really interesting in terms of, brain energy and just energy in general, is the research looking at creatine in terms of enhancing cognition.

So in terms of supplementation, there are a number of things that have been discussed over the last decade. So magnesium omega threes, multivitamins, all of these have some data support of brain function.

But what we don't generally see is a benefit to healthy people in terms of enhancing brain function. And what a recent, review found is that even in healthy people, consuming creatine in the form of creatine monohydrate at a dose of around five grams a day was linked to improvement across multiple metrics of cognition.

Now, I'm not saying this is somebody who sells creatine, I do not. But what I am thinking is super interesting is recent paper that just came out this year showed that people who were sleep deprived had benefits to cognition when they took creatine, and this was linked to changes in brain energetics because creatine, is phosphorylated and then basically adds a phosphate group to recreate ATP central energy currency.

And a number of studies now show that in a host of brain diseases, there is a drop off in the brain's metabolic state. And so this provides some potential hope is is not necessarily been studied, extensively, but that in states of metabolic dysfunction within the brain, creatine might provide an additional way to get fuel to brain cells.

So just a consideration there. There's a lot to say as far as personal love that. Yeah. We use creatine all the time. You know, the thing is that many people yeah we use it all the time.

The other thing is and we also do blood flow restriction training for lower extremities. Right. Because that even boosts the body enough even more. So we're big fans of all of that.

That being said, you know, as a cardiologist, we do like cardio and we know VO2 max is correlated to lots of good things in you 100%. So it's not about it's not an either or just as you're listening to this.

But the creatine is is wonderful. And it's also good for muscle function. So if you want to actually take creatine, I don't know how you do it, but we tend to say creatine before we work out.

So have more energy in the muscle and then you can take it for your brain as well. Right. So yeah, we love we love all that. So. Well, well, I'm going to say you know the balance here being I think aerobic conditioning has been historically seen as central to health.

And it is. But the thing that most people don't talk about is that the weight training is also key specific to brain health because of some of these machines and the metabolic benefit we get from it.

And I also will just say in terms of the creatine, 95% of it is located in your skeletal muscles and the majority of the data over the last decades. This is not new science.

Again shows aerobic benefits. Or I should just say, exercise benefits of strength, conditioning benefits. So that to me seems like an additional, enhancement of health.

And it may be the case that creatine supplementation is good for the brain, not just because it's able to create more energy in the brain that because, as you said, it does something really advantageous to muscles.

Maybe we could talk just very briefly about a couple of, a food based thing because I know that's always popular to people, but, you. Know, I'm sure. Yeah.

Let me just say one last thing about creating, a lot of people have heard about the MTA for mutation, and people have different, difficulty methylation, right.

Which is basically adding this carbons with three hydrogens on to other molecules. Right. To be able to detox, be able to make neurotransmitters and things like that.

And if you don't have enough of that, homocysteine builds up in your system and that can increase clotting. That's been associated with cardiovascular disease.

Well, it turns out a lot of the body's methylation, capacity goes to making creatine. So if you're actually substituting or supplementing with creatine, you actually decrease the demand on your methylation system to make methyl groups for that purpose.

And therefore you're actually able to get your you can actually treat your for not only with methylated folate and folic acid and B12 and B6, the other things that you need.

But the creatine also will help in that regard, which is a pretty cool thing. So, just thought I'd throw that in there.

Diet, alcohol, and sleep quality

Yeah. Awesome bonus. Yeah. So maybe here in the last little bit, just make a couple of comments about diet. So I think as you've already alluded to, diet is central to overall health, to brain health, to longevity.

And by and large, I'm a proponent of, you know, making small changes rather than assuming you've got to go keto or do something intense unless you're working with a practitioner, because if you look at long term sustainability, it's usually about things that people enjoy and are able to stick to you.

So trying to make small changes to deviate away from the standard American diet that's highly processed, very important. But one topic within this conversation that I find fascinating is the conversation around alcohol, longevity and dementia.

So there are a variety of different opinions on alcohol, and they may be organ specific. So you may have different opinions related to heart health than I do related to brain health.

And it may be the case that there are different. However, a couple of things I'll just say around this. One is it's been proven in cell studies primarily that alcohol is a neurotoxin, meaning if you expose a neuron to alcohol, it will basically kill the neuron.

That doesn't necessarily mean that's what's happening in the brain. However, there are conditions, for example, alcohol related dementia, which show a very clear correlation.

High levels of alcohol consumption can lead to dementia. We know alcohol impairs key vitamins related to brain health, like B12. And we know that some of the mechanisms in which alcohol may damage brain health.

So this is certainly looking at longevity because alcohol related brain damage is not a transient thing necessarily would include metabolic, immune and neuroplasticity mechanism.

So hits on all of these three things. With that said, some of the largest data sets suggest that at smaller doses of alcohol, so 1 to 2 drinks a day, there may be a decreased risk for dementia in certain populations.

And the largest study I'm aware of, I think, came out of South Korea, and it showed that people who drank a little bit of alcohol had lower risk of dementia than people who didn't drink alcohol at all.

There's some considerations around an abstinence bias and whether there social interactions. But one thing that I want to make clear that most people don't understand is that there are some surrogates, you know, surrogates, again, we're going to use that term, but in a positive way here.

There are some surrogates that can tell you whether you may be experiencing brain issues as a reflection of alcohol consumption. And I think these are really, really important for people to consider.

So what would tell you that your brain is experiencing damage from alcohol consumption without needing to get an MRI, without finding yourself with the diagnosis?

Brownouts and blackouts, which are actually quite common, especially in younger people or anybody who binge drinks alcohol, which is kind of defined by drinking a number of drinks in one period.

These are markers of brain risk. So people who experience these things are at higher risk of developing brain conditions. And maybe the more important one for everyone else listening out there who's trying to figure out whether it's an issue hangover.

So what is a hangover? Usually we think about a hangover. As you know, you had too much alcohol. Maybe you're dehydrated. The reality is that a hangover is a surrogate for inflammation in your bloodstream, and therefore damage to your brain is a function of neuroinflammation.

When they have done research looking at the correlations between being hangover and inflammatory markers, what they found is that the severity of hangover is correlated with inflammatory responses in the bloodstream, and in particular with levels of interleukin six, tumor necrosis factor alpha and C reactive protein.

So those are a couple of technical terms. But what I would tell people here is your body and in particular your brain. It's often giving you the data you need in order to determine whether what you're doing in your life is a net positive or a net negative in terms of brain function.

So feeling really sleepy is an indicator that your brain didn't get enough sleep. So what will it matters? Because not getting good sleep is a strong predictor of developing conditions like dementia, mental health conditions, and overall having worse cognition.

Feeling hung over is not just oh, I'm dehydrated. It is actually a risk factor for having higher levels of inflammation, which correlate with worse brain health.

So the main point I'm making here is you need to pay attention to what your brain is telling you. And as it relates to alcohol, there are some really powerful signals that we can all intuit, which can also tell us about our body's ability to process what can be, at higher levels, a toxin.

So certainly I'm in favor of a generally, minimally processed diet rich in fruits and vegetables, low and ultra processed foods, added sugars, all of that stuff.

And I think you can kind of go into any of these more specific components of the diet. But one question to be asking is, how does my brain feel and use that as a bit of a guidepost when we get to molecules like alcohol or ethanol in particular, that certainly people metabolize differently and can have different risk factors depending on who we are.

Yeah, I think that's I think that's very well said. And we know there's some genetic predispositions for alcohol impact too, whether you're ApoE e4 or whether you're opposed to some people who actually benefit a little bit more from a little bit of alcohol, nobody benefits from a lot of alcohol.

ApoE4 is really should stay away from it all together. A little bit of alcohol. I drank a little bit of alcohol and kombucha. I never drank alcohol per se, because it does increase, alcohol dehydrogenase in the liver, which has been shown when it's elevated to actually improve longevity.

It breaks down other molecules besides just alcohol, certain alcohol, substances in the body. And so that's interesting in and of itself. But to your point, I think you should gauge this.

And if you are having issues with alcohol, either your sleep is affected and we find almost anybody that drinks, even one glass of wine. Their sleep is affected based on their willpower or rank.

So if you're, if you're, if you're if you're thinking that I'm using alcohol to calm myself. Right. The other interesting thing is genetically, there are people that actually wake up the next morning with much higher levels of anxiety.

It calms them in the short term, but they're much more anxious the next day. So if you're experiencing more anxiety the day after your drink, or the blackouts or the fogginess or all the other things that that Austin's been talking about here, you know, those are real things to pay attention to.

So very, very cool. I think that that's so key. Maybe one last point on that. So as I mentioned many times, sleep quality is one of the best predictors of basically every health outcome.

This isn't to say necessarily that if you're not getting good sleep, you're going to be able to pin down and say, this is the reason for it. But one of the greatest myths is that being sedated or being unconscious is equivalent to getting good quality sleep.

And what many people have done. And really, the origin of the whole nightcap is this idea that you're going to take some alcohol or you're going to consume some alcohol.

It's going to be a central nervous system depressant, and you will pass out and therefore get good sleep. But when you look at sleep architecture for people who have consumed alcohol before bed, what you realize is that the sleep cycles of deep sleep do not correlate with healthy patterns.

And therefore, because you're disrupting sleep architecture, you're not actually getting the quality of sleep you would have if you were going to get to sleep.

Using non alcohol related means. And so this is just I think a very pervasive myth is that if you're unconscious, it's quality sleep. The reality is if you're using alcohol to sedate yourself, to go to sleep, you really want to look at the reasons why you're using that.

And probably if you can, because we all know that alcohol can create a number of issues with withdrawal,

especially if you're using it at high levels.

But this is the type of scenario where you really need to work on the the drivers of this, potentially with your practitioner. But if you're somebody who's using a glass of wine before bed or something in order to fall asleep, don't expect that that is quality sleep.

That's right. You know, the other interesting thing that you pointed out is that it does disrupt slow wave sleep and slow sleep, restorative sleep. And that's when your lymphatic pathway is working.

Actually. That's when you're actually draining all of the toxins out of your brain from the day prior. So you're actually robbing yourself of your ability to detox your brain the way you normally would after you've added more toxins to it.

So it's kind of a double whammy, if you will. When you drink alcohol. So there's many, many downsides to consuming alcohol. Austin. It's been an amazing conversation that we could go on for another hour and a half, probably.

But, I really appreciate you taking the time to, to enlighten us from, you know, your vantage point here. Really? Yeah. So I completely enjoyed it as well.

Thanks so much for having me. Absolutely.